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CCAATCGCCCGGTGCGGTGGTGCAGGGTCTCGGGCTAGTCATGGCGTCCCCGTCTCGGAGAC
TGCAGACTAAACCAGTCATTACTTGTTTCAAGAGCGTTCTGCTAATCTACACTTTTATTTTC
TGGATCACTGGCGTTATCCTTCTTGCAGTTGGCATTTGGGGCAAGGTGAGCCTGGAGAATTA
CTTTTCTCTTTTAAATGAGAAGGCCACCAATGTCCCCTTCGTGCTCATTGCTACTGGTACCG
TCATTATTCTTTTGGGCACCTTTGGTTGTTTTGCTACCTGCCGAGCTTCTGCATGGATGCTA
AAACTGTATGCAATGTTTCTGACTCTCGTTTTTTTGGTCGAACTGGTCGCTGCCATCGTAGG
ATTTGTTTCAGACATGAGATTAAGAACAGCTTTAAGAATAATTATGAGAAGGCTTTGAAGC
AGTATAACTCTACAGGAGATTATAGAAGCCATGCAGTAGACAAGATCCAAAATACGTTGCAT
TGTTGTGGTGTCACCGATTATAGAGATTGGACAGATACTAATTATTACTCAGAAAAAGGATT
TCCTAAGAGTTGCTGTAAACTTGAAGATTGTACTCCACAGAGAGATGCAGACAAAGTAAACA
ATGAAGGTTGTTTTATAAAGGTGATGACCATTATAGAGTCAGAAATGGGAGTCGTTGCAGGA
ATTTCCTTTGGAGTTGCTTGCTTCCAACTGATTGGAATCTTTCTCGCCTACTGCCWCTCTCG
TGCCATAACAAATAACCAGTATGAGATAGTGTAACCCAATGTATCTGTGGGCCTATTCCTCT
CTACCTTTAAGGACATTTAGGGTCCCCCCTGTGAATTAGAAAGTTGCTTGGCTGGAGAACTG
ACAACACTACTTACTGATAGACCAAAAAACTACACCAGTAGGTTGATTCAATCAAGATGTAT
GTAGACCTAAAACTACACCAATAGGCTGATTCAATCAAGATCCGTGCTCGCAGTGGGCTGAT
TCAATCAAGATGTATGTTTGCTATGTTCTAAGTCCACCTTCTATCCCATTCATGTTAGATCG
TTGAAACCCTGTATCCCTCTGAAACACTGGAAGAGCTAGTAAATTGTAAATGAAGT

(57) Abstract

Membrane–bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor–ligand interactions. The membrane–bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane–bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identifiy the coding sequences for novel receptor or membrane–bound proteins. The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

FURTHER PRO POLYPEPTIDES AND SEQUENCES THEREOF

FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

BACKGROUND OF THE INVENTION

Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci. 93:7108-7113 (1996); U.S. Patent No. 5,536,637)].

Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesin molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

1. **PRO1560**

The tetraspan family of proteins has grown to include approximately 20 known genes from various species, including drosophila. The tetraspans are also known as the transmembrane 4 (TM4) superfamily and are proposed to have an organizing function in the cell membrane. Their ability to interact with other molecules and function in such diverse activities as cell adhesion, activation and differentiation, point to a role of aggregating large molecular complexes. Skubitz, et al., J. Immunology, 157:3617-3626 (1996). The tetraspan group has also emerged as a set of proteins with prominent functions in Schwann cell biology. Mirsky and Jessen, Curr. Opin. Neurobiol., 6(1):89-96 (1996). Tetraspans (also sometimes called tetraspanins) are further described in Maecker, et al., FASEB, 11:428-442 (1997). Thus, members of the tetraspan family are of interest.

2. **PRO444**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO444.

3. **PRO1018**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1018.

4. **PRO1773**

The primary and rate-limiting step in retinoic acid biosynthesis requires the conversion of retinol to retinal. Retinol dehydrogenase proteins are enzymes which function to recognize holo-cellular retinol-binding protein as a substrate, thereby catalyzing the first step of retinoic acid biogenesis from its substrate. Various retinol dehydrogenase genes have been cloned and characterized, wherein the products of these genes are suggested as potentially being useful for the treatment of retinitis pigmentosa, psoriasis, acne and various cancers (Chai et al., J. Biol. Chem. 270:28408-28412 (1995) and Chai et al., Gene 169:219-222 (1996)). Given the obvious importance of the retinol dehydrogenase enzymes, there is significant interest in the identification and

characterization of novel polypeptides having homology to a retinol dehydrogenase. We herein describe the identification and characterization of novel polypeptides having homology to a retinol dehydrogenase protein, designated herein as PRO1773 polypeptides.

5. PRO1477

Glycosylation is an important mechanism for modulating the physiochemical and biological properties of proteins in a stage- and tissue-specific manner. One of the important enzymes involved in glycosylation in Saccharomyces cerevisiae is alpha 1,2-mannosidase, an enzyme that catalyzes the conversion of Man9GlcNAc2 to Man8GlcNAc2 during the formation of N-linked oligosaccharides. The Saccharomyces cerevisiae alpha 1,2-mannosidase enzyme of is a member of the Class I alpha 1,2-mannosidases that are conserved from yeast to mammals. Given the important roles played by the alpha 1,2-mannosidases and the mannosidases in general in glycosylation and the physiochemical activity regulated by glycosylation, there is significant interest in identifying novel polypeptides having homology to one or more mannosidases. We herein describe the identification and characterization of novel polypeptides having homology to a mannosidase protein, designated herein as PRO1477 polypeptides.

6. PRO1478

Recently, a new subfamily of galactosyltransferase genes that encode type II transmembrane proteins was identified from a mouse genomic library (Hennet et al., (1998) *J. Biol. Chem.* 273(1):58-65). Galactosyltransferases, in general, are all of interest. Beta 1,4-galactosyltransferase is been found in two subcellular compartments where it is believed to perform two distinct function. Evans, et al., Ioessays, 17(3):261-268 (1995). Beta 1,4-galactosyltransferase is described as a possible transducing receptor in Dubois and Shur, Adv. Exp. Med. Biol., 376:105-114 (1995), and further reported on in Shur, Glycobiology, 1(6):563-575 (1991). Expression and function of cell surface galactosyltransferase is reported on in Shur, Biochim. Biophys. Acta., 988(3):389-409 (1989). Moreover, the receptor function of galactosyltransferase during mammalian fertilization is described in Shur, Adv. Exp. Biol., 207:79-93 (1986), and the receptor function during cellular interactions is described in Shur, Mol. Cell Biochem., 61(2):143-158 (1984). Thus, it is understood that galactosyltransferases and their related proteins are of interest.

7. PRO831

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO831.

8. PRO1113

Protein-proteininteractions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein

sequence of amino acid residues from about 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1773 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1773 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1773 polypeptide by contacting the native PRO1773 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1773 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

5. PRO1477

A cDNA clone (DNA56529-1647) has been identified, having homology to nucleic acid encoding a mannosidase protein that encodes a novel polypeptide, designated in the present application as "PRO1477".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1477 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from about 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1477 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 23 and about 2119, inclusive, of Figure 9 (SEQ ID NO:11). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 540 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1477 polypeptide, with or without and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 21 to about amino acid position 40 and from about amino acid position 84 to about amino acid position 105 in the PRO1477 amino acid sequence (Figure 10, SEQ ID NO:12).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1477 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 9 (SEQ ID NO:11).

In another embodiment, the invention provides isolated PRO1477 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1477 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 699 of Figure 10 (SEQ ID NO:12).

In another aspect, the invention concerns an isolated PRO1477 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

In a further aspect, the invention concerns an isolated PRO1477 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

In yet another aspect, the invention concerns an isolated PRO1477 polypeptide, comprising the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or a fragment thereof sufficient to provide a binding site for an anti-PRO1477 antibody. Preferably, the PRO1477 fragment retains a qualitative biological activity of a native PRO1477 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from about 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1477 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1477 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1477 polypeptide by contacting the native PRO1477 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1477 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

6. **PRO1478**

A cDNA clone (DNA56531-1648) has been identified that encodes a novel polypeptide having sequence identity with galactosyltransferase and designated in the present application as "PRO1478."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1478 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1478 polypeptide having the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1478 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 77 and about 1057, inclusive, of Figure 11 (SEQ ID NO:16). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203286

deposit no. 203478.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 8 (SEQ ID NO:10), evidenced significant homology between the PRO1773 amino acid sequence and the following Dayhoff sequences: ROH2_RAT, ROH3_RAT, AF030513_1, ROH1_RAT, AF056194_1, AF057034_1, P_W18337, P_W18328, BDH_HUMAN and BDH_RAT.

EXAMPLE 8: Isolation of cDNA clones Encoding Human PRO1477

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52641. Based on the DNA52641 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO240.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGCCAGAAGGGCGTGATTGACGTC-3' (SEQ ID NO:13)

reverse PCR primer 5'-CCATCCTTCTTCCCAGACAGGCCG-3' (SEQ ID NO:14)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52641 sequence which had the following nucleotide sequence

hybridization probe

5'-GAAGCCTGTGTCCAGGTCCTTCAGTGAGTGGTTTGGCCTCGGTC-3' (SEQ ID NO:15)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO240 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1477 (designated herein as DNA56529-1647 [Figure 9, SEQ ID NO:11]; and the derived protein sequence for PRO1477.

The entire nucleotide sequence of DNA56529-1647 is shown in Figure 9 (SEQ ID NO:11). Clone DNA56529-1647 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 23-25 and ending at the stop codon at nucleotide positions 2120-2122 (Figure 9). The predicted polypeptide precursor is 699 amino acids long (Figure 10). The full-length PRO240 protein shown in Figure 10 has an estimated molecular weight of about 79,553 daltons and a pI of about 7.83. Analysis of the full-length PRO1477 sequence shown in Figure 10 (SEQ ID NO:12) evidences the presence of the following: transmembrane domains from about amino acid 21 to about amino acid 40 and from about amino acid 84 to about amino acid 105. Clone DNA56529-1647 has been deposited with ATCC on September 29, 1998 and is assigned ATCC deposit no. 203293.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 10 (SEQ ID NO:12), evidenced significant

homology between the PRO1477 amino acid sequence and the following Dayhoff s quences: CELT03G11_1, CEZC410_4, A54408, SSMAN9MAN_1, GEN12643, GEN12642, AF027156_1, P_W46900, SPAC23A1_4 and DMC86E4_5.

EXAMPLE 9: Isolation of cDNA clones Encoding Human PRO1478

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA52719". Based on the DNA52719 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1478.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'GCGAACGCTTCGAGGAGTCCTGG3' (SEQ ID NO:18); and

reverse PCR primer 5'GCAGTGCGGGAAGCCACATGGTAC3' (SEQ ID NO:19).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensusDNA52719 sequence which had the following nucleotide sequence:

hybridization probe 5'CTTCCTGAGCAGGAAGAAGATCCGGCACCACATCTACGTGCTCAAC3'(SEQ ID NO:20).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1478 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1478 and the derived protein sequence for PRO1478.

The entire coding sequence of PRO1478 is included in Figure 11 (SEQ ID NO:16). Clone DNA56531-1648 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and an apparent stop codon at nucleotide positions 1058-1060 of SEQ ID NO:16. The predicted polypeptide precursor is 327 amino acids long. The type II transmembrane sequence is believed to be at about amino acids 29-49 of SEQ ID NO:17, and an N-glycosylation site is believed to be at about amino acids 154-157 of SEQ ID NO:17. Clone DNA56531-1648 has been deposited with ATCC and is assigned ATCC deposit no. 203286. The full-length PRO1478 protein shown in Figure 12 has an estimated molecular weight of about 37,406 daltons and a pI of about 9.3.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:17), revealed sequence identity between the PRO1478 amino acid sequence and the following Dayhoff sequences: YNJ4_CAEEL, P_R55706, A38781_1, NALS_MOUSE, HUMHGT_1, AF048687_1, CEW02B12_11, Y09F_MYCTU, FOJO_DROME, and G01936.

or antagonist thereof as hereinbefore described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO1560 (UNQ767) cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA19902-1669". The start and stop codons are shown in bold and underlined font.

Figure 2 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in Figure 1.

Figure 3 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO444 (UNQ328) cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA26846-1397". The start and stop codons are shown in bold and underlined font.

Figure 4 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in Figure 3.

Figure 5 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO1018 (UNQ501) cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA56107-1415". The start and stop codons are shown in bold and underlined font.

Figure 6 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in Figure 5.

Figure 7 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO1773 (UNQ835) cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA56406-1704". The start and stop codons are shown in bold and underlined font.

Figure 8 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in Figure 7.

Figure 9 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO1477 (UNQ747) cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA56529-1647". The start and stop codons are shown in bold and underlined font.

Figure 10 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in Figure 9.

Figure 11 shows a nucleotide sequence (SEQ ID NO:16) of a native sequence PRO1478 (UNQ748) cDNA, wherein SEQ ID NO:16 is a clone designated herein as "DNA56531-1648". The start and stop codons are shown in bold and underlined font.

Figure 12 shows the amino acid sequence (SEQ ID NO:17) derived from the coding sequence of SEQ ID NO:16 shown in Figure 11.

Figure 13 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO831 (UNQ471) cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA56862-1343". The start and stop codons are shown in bold and underlined font.

FIGURE 9

GCGGGCTGTTGACGGCGCTGCGATGGCTGCCTGCGAGGGCAGGAGAAGCGGAGCTCTCGGTT
CCTCTCAGTCGGACTTCCTGACGCCGCCAGTGGGCGGGGCCCCTTGGGCCGTCGCCACCACT
GTAGTCATGTACCCACCGCCGCCGCCGCCGCCTCATCGGGACTTCATCTCGGTGACGCTGAG
CTTTGGCGAGAGCTATGACAACAGCAAGAGTTGGCGGCGGCGCTCGTGCTGGAGGAAATGGA
AGCAACTGTCGAGATTGCAGCGGAATATGATTCTCTTCCTCCTTGCCTTTCTGCTTTTCTGT
GGACTCCTCTTCTACATCAACTTGGCTGACCATTGGAAAGCTCTGGCTTTCAGGCTAGAGGA
AGAGCAGAAGATGAGGCCAGAAATTGCTGGGTTAAAACCAGCAAATCCACCCGTCTTACCAG
CTCCTCAGAAGGCGGACACCGACCCTGAGAACTTACCTGAGATTTCGTCACAGAAGACACAA
AGACACATCCAGCGGGGACCACCTCACCTGCAGATTAGACCCCCAAGCCAAGACCTGAAGGA
TGGGACCCAGGAGGAGGCCACAAAAAGGCAAGAAGCCCCTGTGGATCCCCGCCCGGAAGGAG
ATCCGCAGAGGACAGTCATCAGCTGGAGGGGAGCGGTGATCGAGCCTGAGCAGGGCACCGAG
CTCCCTTCAAGAAGAGCAGAAGTGCCCACCAAGCCTCCCCTGCCACCGGCCAGGACACAGGG
CACACCAGTGCATCTGAACTATCGCCAGAAGGGCGTGATTGACGTCTTCCTGCATGCATGGA
AAGGATACCGCAAGTTTGCATGGGGCCATGACGAGCTGAAGCCTGTGTCCAGGTCCTTCAGT
GAGTGGTTTGGCCTCGGTCTCACACTGATCGACGCGCTGGACACCATGTGGATCTTGGGTCT
GAGGAAAGAATTTGAGGAAGCCAGGAAGTGGGTGTCGAAGAAGTTACACTTTGAAAAGGACG
TGGACGTCAACCTGTTTGAGAGCACGATCCGCATCCTGGGGGGGCTCCTGAGTGCCTACCAC
CTGTCTGGGGACAGCCTCTTCCTGAGGAAAGCTGAGGATTTTGGAAATCGGCTAATGCCTGC
CTTCAGAACACCATCCAAGATTCCTTACTCGGATGTGAACATCGGTACTGGAGTTGCCCACC
CGCCACGGTGGACCTCCGACAGCACTGTGGCCGAGGTGACCAGCATTCAGCTGGAGTTCCGG
GAGCTCTCCCGTCTCACAGGGGATAAGAAGTTTCAGGAGGCAGTGGAGAAGGTGACACAGCA
CATCCACGGCCTGTCTGGGAAGAAGGATGGGCTGGTGCCCATGTTCATCAATACCCACAGTG
GCCTCTTCACCCACCTGGGCGTATTCACGCTGGGCGCCAGGGCCGACAGCTACTATGAGTAC
CTGCTGAAGCAGTGGATCCAGGGCGGGAAGCAGGAGACACAGCTGCTGGAAGACTACGTGGA
AGCCATCGAGGGTGTCAGAACGCACCTGCTGCGGCACTCCGAGCCCAGTAAGCTCACCTTTG
TGGGGGAGCTTGCCCACGGCCGCTTCAGTGCCAAGATGGACCACCTGGTGTGCTTCCTGCCA
GGGACGCTGGCTCTGGGCGTCTACCACGGCCTGCCCGCCAGCCACATGGAGCTGGCCCAGGA
GCTCATGGAGACTTGTTACCAGATGAACCGGCAGATGGAGACGGGGCTGAGTCCCGAGATCG
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CACAACCTGCTGCGGCCAGAGACCGTGGAGAGCCTGTTCTACCTGTACCGCGTCACAGGGGA
CCGCAAATACCAGGACTGGGGCTGGGAGATTCTGCAGAGCTTCAGCCGATTCACACGGGTCC
CCTCGGGTGGCTATTCTTCCATCAACAATGTCCAGGATCCTCAGAAGCCCGAGCCTAGGGAC
AAGATGGAGAGCTTCTTCCTGGGGGAGACGCTCAAGTATCTGTTCTTGCTCTTCTCCGATGA
CCCAAACCTGCTCAGCCTGGACGCCTACGTGTTCAACACCGAAGCCCACCCTCTGCCTATCT
GGACCCCTGCCTAGGGTGGATGGCTGCTGGTGTGGGGACTTCGGGTGGGCAGAGGCACCTTG
CTGGGTCTGTGGCATTTTCCAAGGGCCCACGTAGCACCGGCAACCGCCAAGTGGCCCAGGCT
CTGAACTGGCTCTGGGCTCCTCCTCGTCTCTGCTTTAATCAGGACACCGTGAGGACAAGTGA
GGCCGTCAGTCTTGGTGTGATGCGGGGTGGGCTGGGCCGCTGGAGCCTCCGCCTGCTTCCTC
CAGAAGACACGAATCATGACTCACGATTGCTGAAGCCTGAGCAGGTCTCTGTGGGCCGACCA
GAGGGGGGCTTCGAGGTGGTCCCTGGTACTGGGGTGACCGAGTGGACAGCCCAGGGTGCAGC
TCTGCCCGGGCTCGTGAAGCCTCAGATGTCCCCAATCCAAGGGTCTGGAGGGGCTGCCGTGA
CTCCAGAGGCCTGAGGCTCCAGGGCTGGCTCTGGTGTTTACAAGCTGGACTCAGGGATCCTC
CTGGCCGCCCCGCAGGGGGCTTGGAGGGCTGGACGGCAAGTCCGTCTAGCTCACGGGCCCCT
CCAGTGGAATGGGTCTTTTCGGTGGAGATAAAAGTTGATTTGCTCTAACCGCAA

FIGURE 10

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56529

><subunit 1 of 1, 699 aa, 1 stop

><MW: 79553, pI: 7.83, NX(S/T): 0

MAACEGRRSGALGSSQSDFLTPPVGGAPWAVATTVVMYPPPPPPPHRDFISVTLSFGESYDN
SKSWRRRSCWRKWKQLSRLQRNMILFLLAFLLFCGLLFYINLADHWKALAFRLEEEQKMRPE
IAGLKPANPPVLPAPQKADTDPENLPEISSQKTQRHIQRGPPHLQIRPPSQDLKDGTQEEAT
KRQEAPVDPRPEGDPQRTVISWRGAVIEPEQGTELPSRRAEVPTKPPLPPARTQGTPVHLNY
RQKGVIDVFLHAWKGYRKFAWGHDELKPVSRSFSEWFGLGLTLIDALDTMWILGLRKEFEEA
RKWVSKKLHFEKDVDVNLFESTIRILGGLLSAYHLSGDSLFLRKAEDFGNRLMPAFRTPSKI
PYSDVNIGTGVAHPPRWTSDSTVAEVTSIQLEFRELSRLTGDKKFQEAVEKVTQHIHGLSGK
KDGLVPMFINTHSGLFTHLGVFTLGARADSYYEYLLKQWIQGGKQETQLLEDYVEAIEGVRT
HLLRHSEPSKLTFVGELAHGRFSAKMDHLVCFLPGTLALGVYHGLPASHMELAQELMETCYQ
MNRQMETGLSPEIVHFNLYPQPGRRDVEVKPADRHNLLRPETVESLFYLYRVTGDRKYQDWG
WEILQSFSRFTRVPSGGYSSINNVQDPQKPEPRDKMESFFLGETLKYLFLLFSDDPNLLSLD
AYVFNTEAHPLPIWTPA

Important features of the protein:

Transmembrane domain:

amino acids 21-40 and 84-105 (type II)

10/270